

REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections of the present application are respectfully requested in view of the amendments to the claims and remarks presented herewith, which place the application into condition for allowance.

Status of the Claims and Formal Matters

Claims 37-54, 56, 58, 59, 61-64 are currently pending in this application. Claim 60 has been withdrawn. In order to advance prosecution and clarify claimed subject matter, claims 37, 38, 40, 42, 43, 45, 46, 47, 49, 54, 56 and 58 have been amended. Amendment to the claims find support throughout the specification as originally filed.

Claim 55 has been cancelled without prejudice, admission, surrender of subject matter or intention of creating estoppel as to equivalents. Applicants hereby assert the right to reclaim withdrawn or cancelled subject matter in co-pending applications. New claims 61-64 have been added. New claims find support in claim 37, original claim 1 and page 12, lines 3-4 of the application as filed. No new matter has been added.

Rejections under §112, 1st paragraph

35 U.S.C. §112, First Paragraph – Enablement

Claims 37-59 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement (Office Action, pages 4-5). The Examiner states that the claims contain subject matter which was not described in the specification in such a way as to enable one of skill in the art to make or use the claimed invention. *Id.* Applicants respectfully traverse the rejections in view of the remarks presented herein and amendments to the claims.

The test for enablement is whether one reasonably skilled in the art could make or use the claimed invention without undue experimentation, based on the disclosure in the application and the information available in the art. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988); MPEP § 2164.01. The Office must consider many factors for enablement, including

the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); MPEP § 2164.01(a).

Applicants respectfully point to the significant guidance and working examples provided in the instant case. The instant application teaches the use of semi-volatile buffers such as ammonium bicarbonate and protein-resistant layers exemplified by polyethylene glycol, dextran, polyurethane, polyacrylamide and self-assembled monolayers (*see inter alia* paragraph [0060] of the published application). Thus, the instant application provides sufficient guidance and working examples to show how to use semi-volatile buffers. *See, e.g.*, MPEP §§2164.01(b), (c), and 2164.02.

Applicants next point to the state of the art at the time of filing. The use of volatile buffers in the field of mass spectrometry was very well known in the art. Applicants respectfully point out to Exhibit 1, Nogami *et al.*, (2005), which provides discussion of the characteristics of such buffers and their use in the field of mass spectrometry. Thus, at the time of filing, the art included well known methods for making and using semi-volatile buffers. *See, e.g., Wands*, 858 F.2d at 740; MPEP §2164.01(a).

Notably, the test for “undue experimentation” is not merely quantitative, and the time and difficulty of experimentation are not determinative. *Wands*, 858 F.2d at 737; MPEP §2164.06. A considerable amount of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance for how the experimentation should proceed. *Wands*, 858 F.2d at 737; MPEP §2164.06. Where an invention involves biological activity, this itself does not constitute “undue experimentation,” particularly where the level of skill is high (as noted in the instant case; *see* Office Action, page 7). *Wands*, 858 F.2d at 740. Furthermore, Applicants need only provide *sufficient* disclosure to teach those of skill in the art how to make and use the claimed invention. MPEP § 2164. The standard does not require thousands of examples or every possible species for the claimed invention. *In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976).

Consequently, based on the knowledge of those skilled in the art at the time of filing, together with the disclosure provided in the instant specification, Applicants respectfully submit that amended claims satisfy the enablement requirement under §112, 1st paragraph. Reconsideration and withdrawal of the §112, 1st paragraph rejection for an alleged failure to comply with the enablement requirement is respectfully requested.

Rejections under § 112, second paragraph.

Claims 37-59 were rejected under 35 U.S.C. §112, 2nd paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In view of the amendments to claims 37, 38, 40, 42, 43, 45, 46, 47, , 49, 54, 56 and 58 and cancellation of claims 55, Applicants urge that this rejection is moot and should be withdrawn.

Rejections under §103(a)

Claims 37-59 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Wagner (WO 00/04382), “Wagner” in view of Kolster. The Applicants respectfully traverse this rejection.

The application relates *inter alia* to sensitive label free detection system, particularly useful in instances where labeled compounds are either not available or where labeling could fundamentally alter the properties of the ligand. The instant label- free method uses mass spectrometry probe. Further, the instant method enables interrogation of enzymatic reactions and the effect compounds have thereon in a label-free manner by desorption and ionization of reactants and product.

Wagner relates to the immobilization of proteins on a mass spectrometry probe and detection of binding events such as antibody binding of epitopes and protein-protein interactions. Wagner does not describe detection of enzyme-mediated catalysis whereby a substrate is converted into a product directly on the probe surface and where the reaction is monitored by detection of products or reactants using mass spectrometry. Wagner does not teach or suggest method of determining the activity of an enzyme by using mass spectroscopy comprising providing a probe carrying an immobilised enzyme; optionally introducing the test compound;

introducing one or more reactants to the immobilised enzyme for a time, and in a form sufficient for a reaction to take place; drying the probe; subjecting the probe to mass spectroscopy; determining the activity of the enzyme, or the effect the test compound had on the activity of the enzyme, by detecting the presence and/or absence of one or more products and/or the one or more reactants; wherein a layer resistant to non-specific protein binding comprising protein repellent molecules is provided on the probe surface.

Kolster does not remedy the deficiencies of Wagner. Kolster relates to standard MALDI for use in DNA diagnostic. However, Kolster is silent with regard to a specific method of determining the activity of an enzyme by using mass spectroscopy comprising providing a probe carrying an immobilised enzyme; optionally introducing the test compound; introducing one or more reactants to the immobilised enzyme for a time, and in a form sufficient for a reaction to take place; drying the probe; subjecting the probe to mass spectroscopy; determining the activity of the enzyme, or the effect the test compound had on the activity of the enzyme, by detecting the presence and/or absence of one or more products and/or the one or more reactants; wherein a layer resistant to non-specific protein binding comprising protein repellent molecules is provided on the probe surface.

Applicants respectfully submit that instant claims are not obvious over Wagner in view of Kolster. Prior art is not limited just to the references being applied, but includes the understanding of one of ordinary skill in the art. The prior art reference (or references when combined) need not teach or suggest all the claim limitations, however, Office personnel must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art.¹

This explanation is lacking with respect to the presently claimed invention.

As stated by the Supreme Court, the framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham v. John Deere Co.*^{2/} The factual inquiries enunciated by the Court are as follows:

¹ MPEP § 2141

^{2/} 383 U.S. 1, 148 USPQ 459 (1966); reaffirmed and relied upon in KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 82 USPQ2d 1385 (2006).

- (1) Determining the scope and content of the prior art;
 - (2) Ascertaining the differences between the claimed invention and the prior art;
- and
- (3) Resolving the level of ordinary skill in the pertinent art.³

As is explained by the Federal Circuit, the motivation to combine is part of the discussion in determining the scope and content of the prior art,^{4/} and where all claim limitations are found in a number of references, the fact finder must determine “[w]hat the prior art teaches... and whether it motivates a combination of teachings from different references.”^{5/} While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation (‘TSM’) test in an obviousness inquiry, the Court acknowledged the importance of identifying ‘a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does’ in an obviousness determination. Moreover, the [Supreme] Court indicated that there is “no necessary inconsistency between the idea underlying the TSM test and the Graham analysis.”^{6/}

Using the above as guidance, Applicants assert that one of ordinary skill in the art would not have had motivation to modify the teachings of Wagner in view of Kolster to arrive at the claimed invention.

Accordingly, since Wagner view of Kolster fails to teach or suggest every element of the claims, Applicants request reconsideration and withdrawal of the rejection under 35 U.S.C. 103(a).

^{3/} *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966); reaffirmed and relied upon in *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 82 USPQ2d 1385 (2006).

^{4/} *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1360, 80 USPQ2d 1641, 1645 (Fed. Cir. 2006); citing *SIBIA Neurosciences, Inc. v. Cadus Pharma. Corp.*, 225 F.3d 1349, 1356 (Fed. Cir. 2000).

^{5/} *Id.* citing *In re Fulton*, 391 F.3d 1195, 1199-1200 (Fed. Cir. 2004).

^{6/} *Takeda*, 492 F.3d at 1356-1357, quoting *KSR*, 127 S.Ct. at 1731.

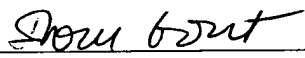
CONCLUSION

Favorable action on the merits is respectfully requested. If any discussion regarding this Response is desired, the Examiner is respectfully urged to contact the undersigned at the number given below, and is assured of full cooperation in progressing the application to allowance.

Applicants believe no additional fees are due with the filing of this Response. However, if any additional fees are required or if any funds are due, the USPTO is authorized to charge or credit Deposit Account Number: **50-0311**, Customer Number: **35437**, Reference Number: **27353-514-US1**.

Respectfully submitted,

Dated: October 2, 2008



Ivor R. Elrifi, Reg. No. 39,529
David Johnson, Reg. No. 41,874
Ilona Gont, Reg. No. 58,714
Attorneys/Agent for Applicants
c/o MINTZ, LEVIN, *et al.*
666 Third Avenue-24th Floor
New York, New York 10017
Telephone: (212) 935-3000
Telefax: (212) 983-3115